REMARKS

Applicant respectfully requests reconsideration.

Claims 1-17, 64, 65, 67 and 72-75 were previously pending in this application.

Claims 15-17 and 67 are canceled without prejudice or disclaimer. Claims 1, 64 and 65 are amended. Claims 1, 64 and 65 are all amended to remove redundant claim language. Claim 64 is further amended to recite that the observed effects are independent of antisense activity. Support for this amendment can be found at least on page 19 line 29 through to page 20 line 2. Claim 65 is amended to recite structural features of the C class CpG immunostimulatory nucleic acid. Support for this amendment can be found on page 24 lines 17-20, page 25 lines 1-5 and 20-23, and page 26 lines 1 and 32-33.

New claims 76-79 are added. Support for new claim 76 can be found at least in previously pending claim 65. Support for new claim 77 can be found in the claims as originally pending (e.g., claim 1) as well as in the specification at least on page 12 lines 7-22, and page 19 line 29 through to page 20 line 2. Support for new claim 78 can be found at least in originally filed claim 8. Support for new claim 79 can be found at least in originally filed claim 14.

As a result, claims 1-14, 65, 65, and 72-79 are pending for examination with claims 1, 64, 65 and 77 being independent claims. No new matter has been added.

Withdrawal of Objections and Rejections

Applicant acknowledges the Examiner's withdrawal of objections to the specification. Applicant further acknowledges the Examiner's conclusion that the claims are enabled and fully supported by the originally filed application (i.e., the claims meet the requirements of 35 U.S.C. § 112, first paragraph, enablement and written description).

Rejection under 35 U.S.C. §103

Claims 1-5, 8-14, 64-65 and 72-75 are rejected under 35 U.S.C. §103(a) as being unpatentable over Witherell et al. as evidenced by and in view of Hanecak et al., as evidenced by Kamal et al. Applicants respectfully traverse in part.

Claims 1 and 77 (and claims dependent thereon) relate to methods for stimulating an immune response in a human subject having an HCV infection that was not successfully treated using a previous non-CpG therapy by administering a CpG immunostimulatory nucleic acid to the subject. Claim 77 further recites that the immune response occurs independently of antisense activity. Claims 64 and 65 (and claims dependent thereon) relate to methods for controlling viral replication and viral spread in a human subject having an HCV infection that was not successfully treated using a previous non-CpG therapy by administering an antiviral agent and a CpG immunostimulatory nucleic acid to the subject. Claim 64 further recites that the effect is independent of antisense activity. Claim 65 further recites that the CpG immunostimulatory nucleic acid is a C class nucleic acid having a semi-soft backbone and comprising two particular sequence motifs.

Witherell summarizes the in vitro and in vivo effects of antisense oligonucleotide ISIS-14803 (5' GTG^{m5}CT^{m5}CATGGTG^{m5}CA^{m5}CGGT^{m5}CT 3'). This oligonucleotide is complementary to the Hepatitis C virus IRES sequence, it comprises a methylated CG dinucleotide, and it has a phosphorothioate backbone. The results summarized by Witherell relate to reduction of HCV RNA and protein levels or viral titer reduction. Witherell speculates that the oligonucleotide may be used as a single agent or in combination therapy with PEGylated interferon and Ribavirin. Witherell further speculates that the oligonucleotide may be used together with other HCV antisense oligonucleotides such as ISIS-6095 in order to overcome certain limitations. Hanecak et al. reports on the antisense activity of ISIS-6095 (5' GCCTTTCGCGACCCAACACT 3'). In particular, Hanecak et al. reports that ISIS-6095 is effective at reducing HCV RNA and protein.

A prima facie case of obviousness has not been made with regards to the pending claims. Accordingly, such claims are not rendered obvious by the combination of references.

For example, Witherell does not teach that ISIS-6095 stimulates an immune response in subjects having an HCV infection, and neither Hanecak et al. nor Kamal et al. provides this teaching either. Moreover, Witherell teaches that antisense oligonucleotides that induce immune cell stimulation are problematic and that oligonucleotides that "elicit less immune stimulation and complement activation" are preferred. (See page 1524, Pharmacology.) Witherell can therefore be reasonably interpreted as teaching away from the use of an antisense oligonucleotide

that stimulates immune responses. Thus, not only does the combination of references not yield each and every limitation of claims 1 and 77 (and claims dependent thereon), one of ordinary skill in the art would have no reasonable expectation of success of using an oligonucleotide that was immunostimulatory in view of the teach away of Witherell. As a result, the combination of references does not render obvious such claims for at least these reasons.

Witherell also does not teach that ISIS-6095 has effects independent of its antisense activity. To the contrary, Witherell chooses ISIS-6095 because of its antisense activity. Neither Hanecak et al. nor Kamal et al. supply this deficiency particularly since Hanecak et al. also highlights ISIS-6095 because of its antisense activity. As a result, the combination of references does not provide all the limitations of claims 64 and 77 and therefore it cannot render obvious such claims for at least this reason.

Witherell, as evidenced by Hanecak et al., also does not teach that oligonucleotide ISIS-6095 has the sequence limitations recited in claim 65 as now amended. For example, ISIS 6095 does not comprise a CGG trinucleotide as recited in claim 65. Kamal et al. does not supply this deficiency. The combination of references therefore does not yield an oligonucleotide having the features recited in claim 65 and this claim (and claims dependent thereon) is not rendered obvious by this combination of references either.

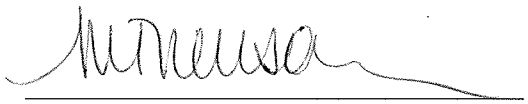
For at least these reasons, the claims are not rendered obvious by the combination of Witherell, Hanecak et al. and Kamal et al. Reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. C1037.70035US01.

Respectfully submitted,



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